

RESPONSE

I. Status of the Claims

Claims 5 and 8 have been cancelled without prejudice and without disclaimer. No claims have been amended. No new claims have been added.

Claims 7, 9 and 10 are therefore presently pending in the case.

II. Rejection of Claims 5 and 7-10 Under 35 U.S.C. § 101

The Action first rejects claims 5 and 7-10 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that claims 5 and 8 lack a patentable utility, as claims 5 and 8 have been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claims 5 and 8 under 35 U.S.C. § 101 is rendered moot. The remainder of this section will therefore focus on claims 7, 9 and 10.

As just one example of the utility of the present nucleotide sequences, the skilled artisan would readily appreciate the utility of tracking expression of the presently claimed sequence. The specification details, at least at page 6, lines 12-14, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of human chromosome 4 (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof

in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such “real world” value that it was acquired by a large pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was \$620 million). The “real world” substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, e.g., Venter *et al.*, 2001, *Science* 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, e.g., Jasny and Kennedy, 2001, *Science* 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner questions this asserted utility, stating that “virtually *any* nucleic acid has utility” in such applications (Action at page 5, emphasis in original). This argument is flawed in at least two respects. First, Applicants submit that only expressed sequences can be used to track gene expression, not just *any* nucleic acid. Expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types, such as cancer cell lines and normal controls. Skilled artisans already have used and continue to use sequences such as Applicants in gene chip applications without further experimentation. Second, the Examiner seems to be confusing the requirements of a specific utility with a unique utility. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: “[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility.” *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

The fact that other nucleotide sequences can be used to track gene expression does not mean that the

use of Applicants' sequence to track gene expression is not a specific utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 3, line 5, the present nucleotide sequence has a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:6 can be used to map a specific region of human chromosome 4, based on the alignment of SEQ ID NO:6 with the chromosome 4 clone described in GenBank Accession Number AC124017 (alignment and first page of the GenBank report are shown in **Exhibit A**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 4 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further

evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions this utility, again stating that "virtually *any* nucleic acid has utility" in such applications (Action at page 5, emphasis in original). However, the Examiner again seems to be confusing the requirements of a specific utility with a unique utility. The fact that other nucleotide sequences can be used to map this specific region of human chromosome 4 does not mean that this use of Applicants' sequence is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "Langer"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Absent such evidence from the Examiner, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "Cross") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C.

§ 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), "Brana"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption".

Brana at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. The Action goes on to state that the claimed sequences lack utility because "further research" (Action at page 5) would be required in certain aspects of the invention. Even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In*

re Angstadt and Griffin, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 5 and 7-10 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

III. Rejection of Claim 5 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. While Applicants in no way agree that the present application does not provide sufficient written description for nucleotide sequences comprising at least 24 contiguous nucleotides from SEQ ID NO:6, as claim 5 has been cancelled without prejudice and without disclaimer, the present rejection of claim 5 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Applicants therefore respectfully request that the rejection of claim 5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Rejection of Claims 5 and 7-10 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 5 and 7-10 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that one skilled in the art would not know how to use the invention as set forth in claims 5 and 8, since claims 5 and 8 have been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claims 5 and 8 under 35 U.S.C. § 112, first paragraph is rendered moot. The remainder of this section will therefore focus on claims 7, 9 and 10.

Applicants submit that as claims 7, 9 and 10 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 7, 9 and 10 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 5 and 7-10 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 5 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 24 contiguous nucleotides of SEQ ID NO:6. Again, while Applicants in no way agree that the present application does not provide enablement for nucleotide sequences comprising at least 24 contiguous nucleotides from SEQ ID NO:6, as claim 5 has been cancelled without prejudice and without disclaimer, the present rejection of claim 5 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Applicants therefore respectfully request that the rejection of claim 5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims 5 and 8 Under 35 U.S.C. § 102(a)

The Action next rejects claims 5 and 8 under 35 U.S.C. § 102(a), as allegedly anticipated by Database Genbank Accession Number AC021985. While Applicants do not necessarily agree with the present rejection, as claims 5 and 8 have been cancelled without prejudice and without disclaimer, Applicants submit that the rejection of claims 5 and 8 under 35 U.S.C. § 102(a) has been rendered moot, and respectfully request withdrawal of the rejection.

VII. Rejection of Claims 5 and 8 Under 35 U.S.C. § 102(a)

The Action next rejects claims 5 and 8 under 35 U.S.C. § 102(a), as allegedly anticipated by Database Genbank Accession Number AC016488. Once again, while Applicants do not necessarily agree with the present rejection, as claims 5 and 8 have been cancelled without prejudice and without disclaimer, Applicants submit that the rejection of claims 5 and 8 under 35 U.S.C. § 102(a) has been rendered moot, and respectfully request withdrawal of the rejection.

VIII. Rejection of Claims 5 and 8 Under 35 U.S.C. § 102(a)

The Action next rejects claims 5 and 8 under 35 U.S.C. § 102(a), as allegedly anticipated by Database Genbank Accession Number AC048370. Once again, while Applicants do not necessarily agree with the present rejection, as claims 5 and 8 have been cancelled without prejudice and without disclaimer, Applicants submit that the rejection of claims 5 and 8 under 35 U.S.C. § 102(a) has been rendered moot, and respectfully request withdrawal of the rejection.

IX. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Steadman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

December 15, 2003

Date

David W. Hibler

David W. Hibler
Agent for Applicants

Reg. No. 41,071

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399

CUSTOMER NUMBER: 24231



RECEIVED

DEC 31 2003

TECH CENTER 1600/2900

Query= SEQ ID NO:6
(255 letters)

Score E
(bits) Value

Sequences producing significant alignments:

AC124017.1.11827.208353 505 e-141

>AC124017.1.11827.208353
Length = 196527

Score = 505 bits (255), Expect = e-141
Identities = 255/255 (100%)
Strand = Plus / Plus

Query: 1 atgttcagggccatccctgtgcatacccaaaagggtttcttccttactaaggcaggta 60
||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 69734 atgttcagggccatccctgtgcatacccaaaagggtttcttccttactaaggcaggta 69793

Query: 61 gaagaggctacgtgttgcataagaaaattgtctttgaggaccaggcactcaccatcaagtt 120
||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 69794 gaagaggctacgtgttgcataagaaaattgtctttgaggaccaggcactcaccatcaagtt 69853

Query: 121 catgttgaggccaaacctgtccacctaagtgcctttgaccacacacttctaccactgg 180
||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 69854 catgttgaggccaaacctgtccacctaagtgcctttgaccacacacttctaccactgg 69913

Query: 181 gaatctgtacaaaaagaggagaatgtgagttattctaacactttgaggataggaaggc 240
||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 69914 gaatctgtacaaaaagaggagaatgtgagttattctaacactttgaggataggaaggc 69973

Query: 241 atcaataaaacctga 255
||||||| |||||
Sbjct: 69974 atcaataaaacctga 69988



NCBI Nucleotide

Entrez PubMed Nucleotide Protein Genome Structure PMC Taxonomy Books

Search **Nucleotide** for

Limits Preview/Index History Clipboard Details

Display default Show: 20

1: AC124017. Homo sapiens BAC ...[gi:27819589]

Links

LOCUS AC124017 138271 bp DNA linear PRI 27-JAN-2003

DEFINITION Homo sapiens BAC clone RP11-317M11 from 4, complete sequence.

ACCESSION AC124017 AC016488

VERSION AC124017.2 GI:27819589

KEYWORDS HTG.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 138271)

AUTHORS Sulston, J.E. and Waterston, R.

TITLE Toward a complete human genome sequence

JOURNAL Genome Res. 8 (11), 1097-1108 (1998)

MEDLINE 99063792

PUBMED 9847074

REFERENCE 2 (bases 1 to 138271)

AUTHORS Cordum, H., Haglund, K., Elliott, G. and Delaney, K.

TITLE The sequence of Homo sapiens BAC clone RP11-317M11

JOURNAL Unpublished (2001)

REFERENCE 3 (bases 1 to 138271)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (06-JUN-2002) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 4 (bases 1 to 138271)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (27-JUN-2002) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 5 (bases 1 to 138271)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (22-JAN-2003) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 6 (bases 1 to 138271)

AUTHORS Waterston, R.

TITLE Direct Submission

JOURNAL Submitted (27-JAN-2003) Department of Genetics, Washington University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Jan 22, 2003 this sequence version replaced gi:21327652.
----- Genome Center
Center: Washington University Genome Sequencing Center
Center code: WUGSC
Web site: <http://genome.wustl.edu/gsc>